REMARKS

There have been no amendments to the specification. Claim 9 has been amended. Claim 24 has been added. Claims 20-23 have been cancelled without prejudice to filing in a subsequent patent application and only for the purpose of avoiding payment of additional claim fees. Upon entry of this amendment claims 1-19 and 24 will be pending in the application. Claims 1-8 and 15-20 were previously withdrawn, under traverse, from consideration based on a restriction of invention so that claims 9-14 and 24 are presently under consideration.

This amendment is being filed under 37 C.F.R. 1.116 governing amendment after final rejection. This amendment is appropriate for entry under Rule 1.116 since it does not raise new issues and places the application in allowable condition and/or places the application in better form for consideration of appeal.

Applicant would like to thank Examiner Meller for the courtesy extended during the telephone conference on January 7, 2004.

The rejection of claims 9-14 under 35 U.S.C. §102(a or e) or under 35 U.S.C. §103 in view of U.S. Patent No. 6,458,760 to Seyfried et al.

Claims 9-14 were rejected under 35 U.S.C. §102(a or e) as having each and every feature and interrelationship anticipated by U.S. Patent No. 6,458,760 to Seyfried et al or in the alternative as being obvious under 35 U.S.C. §103 over the Seyfried reference.

"It is elementary that an anticipation rejection requires a showing that each limitation of a claim must be found in a single reference, practice, or device." See In re Donohue, 226 USPQ 619, 621 point 2 (Fed. Cir. 1985).

As stated in MPEP §2143, to establish a *prima facie* case of obviousness, *inter alia*, the prior art reference (or references when combined) must teach or suggest all the claim limitations.

Applicant's claim 9 recites: "A method for treating neurodegeneration in a subject suffering from neurodegeneration, comprising: administering to the subject a therapeutically effective amount of a lysosomal modulating compound, a physiologically

acceptable salt of the lysosomal modulating compound or a combination thereof, wherein enzymatic capacity of lysosomes in the subject is enhanced."

As an initial matter, the Seyfried reference appears to use specific chemical compounds to inhibit the activity of enzymes that are released from lysosomes into the cell cytoplasm. Release of enzymes into the cell is considered by Seyfried to be undesirable because once released the enzymes cleave structural components within the cell and thereby facilitate cell death. Thus, Seyfried attempts to inhibit the released enzymes to reduce cellular component damage.

Applicant uses the claimed compounds to upregulate enzymatic activity inside the lysosomes. See claim 9, which recites in one pertinent part, with underlining added: ". . . wherein enzymatic capacity <u>of lysosomes</u> in the subject is enhanced." The enhanced enzymatic capacity within the lysosome reduces lysosomal accumulation of structural breakdown products that can lead to lysosomal dysfunction. Claims 9-14 and 24 are not anticipated or obvious over the Seyfried reference and are patentable for at least this reason.

The Seyfried reference appears to be limited to "a method for treating tissue damage caused by ischemia in a patient". See, for example the abstract and column 3, lines 19-20 therein. The Seyfried reference does not teach or suggest the treatment of neurodegeneration in a subject suffering from at least one of Alzheimer's disease, Parkinson's disease or lysosomal storage disorders. Claims 9-14 and 24 are not anticipated or obvious over the Seyfried reference and are patentable for at least this additional reason.

<u>The rejection of claims 9-14 under 35 U.S.C. §102(a or e) or under 35 U.S.C. §103 in view of document WO 00/56335 to Ellman et al.</u>

Claims 9-14 were rejected under 35 U.S.C. §102(a or e) as having each and every feature and interrelationship anticipated by International Publication Number WO 00/56335 to Ellman et al or in the alternative as being obvious under 35 U.S.C. §103 over the Ellman reference.

The Ellman reference does not teach or suggest Applicant's claim ed invention.

The Ellman application does not teach or suggest administering Z-Phe-Ala-diazomethylketone (ZPAD, also known as PADK) for treating neurodegeneration in a subject suffering from neurodegeneration. Rather, the Ellman document merely uses Z-Phe-Ala-diazomethylketone at sufficiently high levels to inhibit cathepsin enzymes and thereby to induce pathogenic protein accumulation in order to show subsequent protective protein clearance with the application of their claimed non-peptide aspartyl protease inhibitors (e.g., EA-1) as shown in Figures 11, 15A, and 16A. In fact, ZPAD treatment is shown to induce cellular accumulation of both tau species (see Figures 10A, 10C, 11, 14A, 14C, and 15A) and fragments of the amyloid precursor protein (Figures 10B and 10D). Since the Ellman document does not teach or suggest use of Z-Phe-Ala-diazomethylketone for treating neurodegeneration in a subject suffering from neurodegeneration, Applicant's claims 9-14 and 24 are patentable for at least this reason.

- **Claim 24 is additionally patentable.**

Claim 24 recites: "The method of claim 9 wherein the therapeutically effective amount of a lysosomal modulating compound, a physiologically acceptable salt of the lysosomal modulating compound or a combination thereof administered to the subject is sufficient to enhance enzymatic capacity of lysosomes but is not sufficient to generate pathogenic accumulations of proteins or protein fragments." As discussed above, the Ellman reference does not teach or suggest the use of Applicant's claimed compounds to treat neurodegeneration in a subject suffering from neurodegeneration. Further, the Ellman reference appears to teach that ZPAD generates pathogenic accumulations of proteins or protein fragments. See page 10, lines 1-7 and FIG. 15 therein. Applicant's claim 24 is not anticipated by, or obvious over, the Ellman reference and is patentable for at least this additional reason.

- **Applicant completed his invention prior to the publication date of the Ellman reference.**

The compounds recited in the claims of the Ellman reference and the compounds claimed by the Applicant do not overlap. Applicant's invention of claims 9-14 and 24 is not the same as that claimed by Ellman.

The Ellman reference has an international filing date of March 24, 2000 and is therefore subject to the pre-AIPA version of 35 USC §102(e). See MPEP §706.02(a), page 700-23, Rev 1, Feb. 2003. The 102(e) date of the Ellman reference therefore appears to be its International Publication Date of 9/28/2000.

The present application claims the benefit of U.S. provisional patent application numbers 60/244,327, filed on 10/30/2000 and 60/254,778, filed on 12/11/2000. Thus, the effective filing date of the present application is less than one year after the 102(e) date of the Ellman reference.

Arguendo, even if the Ellman reference (International Publication No. WO 00/56335) can be prior art, Applicant submits herewith a DECLARATION UNDER 37 C.F.R. 1.131 and attached Exhibits A and B. The Exhibits contain facts showing a completion of the present invention in the United States prior to the September 28, 2000 International Publication Date of the Ellman reference.

In summary, Applicants have addressed each of the objections and rejections within the present Office Action. It is believed the application now stands in condition for allowance, and prompt favorable action thereon is respectfully solicited. The Examiner is invited to telephone Applicant's attorney if it is deemed that a telephone conversation will hasten prosecution of this application.

Respectfully submitted,

Ben A. Bahr

By: _____
James E. Piotrowski
Registration No. 43,860
Alix, Yale & Ristas, LLP
Attorney for Applicants

Date: 1/20/2004
750 Main Street- Suite 1400
Hartford, CT 06103-2721
(860) 527-9211

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